

Amendment to the Claims

1-16. Canceled

17. (Currently amended) A method of delivering an active agent into the central nervous system of an animal comprising administering to said animal a conjugate comprising said agent conjugated to a ~~megalin-binding~~ RAP polypeptide consisting of fragment that comprises an amino acid sequence at least 80% identical to amino acids 221-323 of RAP (SEQ ID NO: 1) (Figure 15), wherein said RAP polypeptide retains megalin-binding activity and wherein said agent is delivered into the central nervous system ~~the transport of said agent conjugated to said megalin-binding RAP fragment across the blood brain barrier of said animal is greater than the transport of said agent in the absence of said conjugation.~~

18. (Currently amended) A method of increasing transcytosis of an active agent across the blood-brain barrier of an animal, comprising administering to said animal a conjugate comprising said agent conjugated to a ~~megalin-binding~~ RAP polypeptide consisting of fragment that comprises an amino acid sequence at least 80% identical to amino acids 221-323 of RAP (SEQ ID NO: 1) (Figure 15), wherein said RAP polypeptide retains megalin-binding activity and wherein said agent is transcytosed across the blood-brain barrier ~~transeytosis of said agent when conjugated to said megalin-binding RAP fragment is greater than the transeytosis of said agent in the absence of said conjugation.~~

19. (Currently amended) A method of treating a disorder of the CNS in a mammal comprising administering to said mammal ~~animal~~ a conjugate comprising an effective amount of a therapeutic agent conjugated to a ~~megalin-binding~~ RAP polypeptide consisting of fragment that comprises an amino acid sequence at least 80% identical to amino acids 221-323 of RAP (SEQ ID NO: 1) (Figure 15).

20. Canceled

21. (Previously presented) The method of claim 19, wherein said disorder is selected from the group consisting of Huntington's Disease, Alzheimer's Disease, Parkinson's Disease, Multiple Sclerosis, Amyotrophic Lateral Sclerosis, ischemia-related disease and stroke, spinal muscular atrophy, cerebellar degeneration, perivenous encephalitis, schizophrenia, epilepsy and a central nervous system cancer.

22. (Withdrawn) The method of claim 21, wherein said disorder is a central nervous system cancer and said agent is a cancer chemotherapeutic agent.

23-57. Canceled

58. (Previously presented) The method of claim 17 or 18 wherein the animal is a human.

59. (Previously presented) The method of claim 58 wherein the human is suffering from a disorder selected from the group consisting of Huntington's Disease, Alzheimer's Disease, Parkinson's Disease, Multiple Sclerosis, Amyotrophic Lateral Sclerosis, ischemia-related disease and stroke, spinal muscular atrophy, cerebellar degeneration, perivenous encephalitis, schizophrenia, epilepsy and a central nervous system cancer.

60. (Previously presented) The method of claim 17 or 18 wherein the agent is a neurotrophic factor.

61. (Previously presented) The method of claim 17 or 18 wherein the therapeutic agent is a neurotrophic factor selected from the group consisting of Glial-Derived Neurotrophic Factor, Nerve Growth Factor, Brain-Derived Neurotrophic Factor, Neurotrophin-3, Neurotrophin-4/5, aFGF, bFGF, CNTF, Leukaemia Inhibitory Factor, Cardiotrophin-1, TGFb, BMPs, GDFs, Neurturin, Artemin, Persephin, EGF, TGFa, Neuregulins, IGF-1, IGF-2, ADNF and PDGF.

62. (Previously presented) The method of claim 17 or 18 wherein the therapeutic agent is brain-derived neurotrophic factor (BDNF).